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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
LANDSMAN, ROBERT S	
ART UNIT	**PAPER NUMBER**
1647	

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/982,543	DIJKE ET AL.	
	Examiner	Art Unit	
	Robert Landsman	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE ____ MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *13 August 2003* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-5,8-10 and 28-40* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-5,8,10 and 28-40* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

1. Formal Matters

A. Amendment A, filed 8/13/03, has been entered into the record. Claims 1-27 were pending. Applicants canceled non-elected claims 6, 7 and 11-27 and added new claims 28-40. Therefore, claims 1-5, 8, 10 and 28-40 are pending and are the subject of this Office Action.

B. All Statutes under 35 USC not found in this Office Action can be found, cited in full, in a previous Office Action.

2. Oath/Declaration

A. The objection to the Oath has been withdrawn in view of Applicants' submission of a supplemental ADS and amending the priority claim in the first line of the specification.

3. Specification

A. All objections to the specification have been withdrawn in view of Applicants' amendments.

4. Claim Objections

A. All objections to the claims have been withdrawn in view of Applicants' amendments.

5. Claim Rejections - 35 USC § 112, first paragraph – scope of enablement

A. Claims 1-5, 8 and 10 remain rejected and new claims 28-40 are also rejected under 35 USC 112, first paragraph, for the reasons already of record on pages 4-5 of the Office Action dated 5/9/03. Applicants argue that there is a striking parallelism between the Wands fact pattern and that claimed invention. Applicants argue that Wands claimed an assay method using an antibody with a desired functional feature (binding affinity) and state that the present invention also provides a functional feature (binding affinity for OP-1 and having 40% homology to residues 23-122 of ALK; encoded by a nucleic acid amplified using primers of SEQ ID NO:12-15, or which hybridizes to bases 256-552 of ALK-6). Applicants argue that, as in Wands, the proteins can be made and tested via combinatorial random mutagenesis and PCR and hybridization can be used to amplify polynucleotides identified by primers or to probe sequences.

Applicants' arguments have been considered, but are not deemed persuasive. First, Applicants state that In re Wands screened and obtained 143 hybridomas. This, respectfully, is a noticeable difference between Wands and the instant invention. Wands had already screened and obtained these hybridomas, whereas the present invention has not obtained nor screened any of the proteins encompassed by the claims, other than SEQ ID NO:4, 6, or 8. Enablement is focused on "make and use" not "make and test." This situation may mimic Wands if Applicants had produced 143 proteins before filing which they had intended to test. However, the Examiner is not stating that this would have overcome any rejection under 35 USC 112, first paragraph, but is stating this only to provide an analogy between the fact pattern of Wands and that of the present invention. Applicants have only identified proteins of SEQ ID NO:4, 6 and 8. Applicants have not screened and identified any other proteins, let alone those having a specific function. The use of combinatorial techniques, while efficient, would still fall under the context of "make and test," not "make and use."

In addition, the hybridomas of Wands were already made and the artisan would know how to use the hybridomas. In contrast, the proteins of the present invention have not been made. Applicants have not identified the critical residues which would be required to produce a functional ALK other than that of the defined residues of SEQ ID NO:4, 6 and 8. In other words, Applicants would not know which residues can be altered to make a protein which is only 40% identical to that of the peptides of claim 1 parts (a)(i-iii), or which is a receptor binding analog of these peptide. Furthermore, in the absence of this guidance and working examples, it would not be predictable to the artisan how to make a functional OP-1 binding peptide other that those disclosed in parts (a)(i-iii) of claim 1. These same arguments are pertinent to the claiming of nucleic acids which can be amplified by PCR, or which hybridize to SEQ ID NO:12-15, or 8, respectively.

The rejection regarding OP-1-mediated biological and cellular responses has been withdrawn in view of the fact that the specification and claims. It is believed that all pertinent arguments have been addressed.

In summary, the breadth of the claims is still excessive regarding Applicants claiming all peptides to be used in the claimed invention which are at least 40% identical to the claimed peptides of SEQ ID NO:4, 6 and 8 or which are OP-1 binding analogs.

6. Claim Rejections - 35 USC § 112, first paragraph – new matter

A. Claims 1-5, 8, 10 and 28-40 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Claim 1 recites "said morphogen being characterized as sharing at least 60% identity or 70% homology to the C-terminal 102 amino acids of SEQ ID NO:7 and being able to substitute for..." Furthermore, Applicants have added claims drawn to specific morphogens (claim 29) and a kit other than that of claim 8. However, Applicants have not pointed out exactly where in the specification support can be found for either of these amendments, including the specific contents of the kit, other than simply referring to a "kit." **This is a new matter rejection**.

7. Claim Rejections - 35 USC § 112, first paragraph – written description

A. Claims 1-5, 8 and 10 remain rejected and new claims 28-40 are also rejected under 35 USC 112, first paragraph, for the reasons already of record on pages 5-6 of the Office Action dated 5/9/03. Applicants argue that Example 9 of the "Revised Interim Written Description Guidelines Training Materials" teaches a situation regarding "hybridization" which is similar to the present invention.

However, there are some differences between these situations. First, the "analysis" in training example states that "the highly stringent hybridization conditions set forth in the claim yield structurally similar DNAs..." This is in contrast to the present situation in which the claims are not drawn solely to molecules which hybridize to a known DNA, but to molecules which are at least 40% identical to known proteins, or fragments thereof, as well as binding analogs and molecules which are identified via the use of primers. Unlike the training example, which states that, due to the conditions used, the molecules identified are structurally similar. On the other hand, molecules which are only 40% identical, or which are "analogs" or which can be amplified are not necessarily structurally similar to the known compounds of the invention (SEQ ID NO:4, 6, and 8). Applicants argue that the situation for "primers" would be similar to that of the training example. However, though the annealing of the primers may occur under stringent conditions, this does not guarantee that the amplified DNA will still be structurally similar to SEQ ID NO:8. Regarding example 13 of the specification, Applicants argue that the present situation does provide structural requirements for the claimed proteins. They argue that the terms "40%" and "binding OP-1" meet these limitations. However, these are not structural limitations. Applicants still have

not taught which amino acid residues can be altered to maintain the structural or binding characteristics of the "variant." The specification provides a written description of only a small number of these constructs. No other species are described, or structurally contemplated, within the instant specification. Therefore, one skilled in the art cannot reasonably visualize or predict critical nucleic acid or amino acid residues which would structurally characterize the genus of proteins claimed, because it is unknown and not described what structurally constitutes this genus, other than "40%" and "binding OP-1," or these protein from any different species, which are further not described.

Furthermore, regarding the claims to molecules which hybridize, Applicants have not provided exact conditions in the claims. The specification only states "exemplary" conditions. Furthermore, the conditions would not be considered "highly" stringent, as required in the training example. A 50 degree wash step would be considered more "moderately" stringent. Therefore, the molecules which hybridize to bases 256-552 of SEQ ID NO:8 would not be expected to be as structurally similar to SEQ ID NO:8 as the molecules identified by the highly stringent conditions in the training example.

The rejection regarding OP-1-mediated biological and cellular responses has been withdrawn in view of the fact that the specification and claims. It is believed that all pertinent arguments have been addressed.

8. Claim Rejections - 35 USC § 112, second paragraph

A. The rejection of claims 1-5 and 8-10 under 35 USC 112, second paragraph, have been withdrawn in view of Applicants' amendment to the claims to recite a conclusion step identifying when the claimed method has been completed.

B. The rejection of claims 1, 2 and 8 under 35 USC 112, second paragraph, has been withdrawn in view of Applicants' argument that one of ordinary skill in the art would understand the meaning of "substantially the same binding affinity."

C. The rejection of claims 1, 2 and 8 under 35 USC 112, second paragraph, has been withdrawn in view of Applicants' amendment to the claims to recite "OP-1 receptor binding analog."

D. Claims 1, 2 and 8 remain rejected under 35 USC 112, second paragraph for the reasons already of record on page 7 of the Office Action dated 5/9/03. Applicants argue that stringent conditions are disclosed in the specification (page 8) and that the first paragraph sets forth an exemplary condition. However, examples of hybridization conditions in the specification are not sufficient to determine the metes and bounds of "stringent." The only way this would be acceptable is if the specification disclosed one specific set of conditions (i.e. not "for example"). Applicants may wish to consider adding the SSC concentration and wash step temperature to the claims, without adding new matter.

E. The rejection of claims 2 and 9 under 35 USC 112, second paragraph, regarding "cellular response" has been withdrawn in view of Applicants' arguments that these responses are well-known in the art.

F. The rejection of claims 4, 5 and 10 under 35 USC 112, second paragraph, has been withdrawn in view of Applicants' addition of a method step to the claims reciting the reporter gene and an explanation that the Type II receptor is essential for some OP-1 receptors.

G. The rejection of claim 5 under 35 USC 112, second paragraph, has been withdrawn in view of Applicants' amendment to the claim to recite "surface receptor protein."

H. The rejection of claim 8 under 35 USC 112, second paragraph, has been withdrawn in view of further consideration by the Examiner. The phrase "candidate analog comprising part of said sample" is clear.

9. Double Patenting

A. Claims 1-5 and 8-10 remain provisionally rejected under the judicially created doctrine of double patenting over one or more claims of copending Application No. 09/267,963. This is a provisional double patenting rejection since the conflicting claims have not yet been patented. Applicants argue that they are not aware of any co-owned U.S. Patent Applications with the above identified serial number. This application is drawn to proteins having serine/threonine kinase domains and nucleic acid molecules encoding these domains. The inventors disclosed are Miyazono, Imamura and Ten Djike, the assignee being the Ludwig Institute for Cancer Research. This application has been passed to issue, but is not available at this time.

10. Claim Rejections - 35 USC § 103

A. All rejections under 35 USC 103 have been withdrawn in view of Applicants' amendment to the claims to recite that the sample used in the methods does not comprise a type II S/T kinase morphogen receptor. Applicants argue that Miyazono et al., a reference used in all of the rejections under 35 USC, does not teach this limitation and, in fact, teaches away from this limitation.

11. Conclusion

A. No claim is allowable. However, it appears that claims 32-40 would be allowable if rewritten to include all the limitations of the claims from which they depend.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Advisory information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Robert Landsman whose telephone number is (703) 306-3407. The examiner can normally be reached on Monday - Friday from 8:00 AM to 5:00 PM (Eastern time) and alternate Fridays from 8:00 AM to 5:00 PM (Eastern time).

If attempts to reach the examiner by telephone are unsuccessful, the Examiner's supervisor, Gary Kunz, can be reached on (703) 308-4623.

Official papers filed by fax should be directed to (703) 308-4242. Fax draft or informal communications with the examiner should be directed to (703) 308-0294.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Robert Landsman, Ph.D.
Patent Examiner
Group 1600
October 21, 2003

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